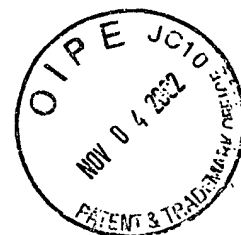


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Applicant(s): H. Robert Horvitz et al.
Filing Date: May 24, 2000 Serial No.: 09/577,897
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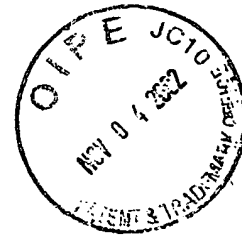
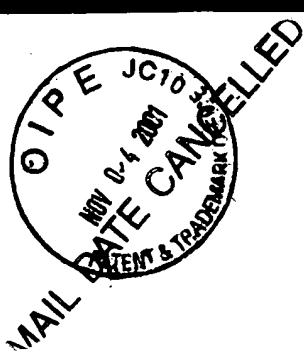
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FIG. 1B

1261 TTGCTGATTTTCCTCGAAGACTACATCGATTTTTCGATAAAATGAGCCAGATCTACTTCGTC 1320
-----+-----+-----+-----+-----+-----+-----+-----+-----+
A D F L E D Y I D F A I N E P D L L R P
90 100
1321 CAGTAGTGATTGCTCCACAATTTTCCCGACAAATGCTCGATAGGAACTATTGCTTGGGA 1380
-----+-----+-----+-----+-----+-----+-----+-----+-----+
V V I A P Q F S R Q M L D R K L L L G N
110 120
T n2274
1381 ATGTTCCAAAACAAATGACATGCTATATTTCGAGAGTATCACGTGGATCGAGTGATCAAAA 1440
-----+-----+-----+-----+-----+-----+-----+-----+-----+
V P K Q M T C Y I R E Y H V D R V I K K
130 140
AGCTCGACGAGATGTGTGATTTAGGTGAGAAAACCTGGAAGCTCTCGTGTATTATAATC
1441 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1500
L D E M C D L D
150
1501 TTGCTTAAACTTCAGACTCCTTTTTCTGTTTCTACACGGCCGAGCTGGATCCGGAAAAT 1560
-----+-----+-----+-----+-----+-----+-----+-----+-----+
S F F L F L H G R A G S G K S
160
CAGTAATTGCATCACAAGCTCTTTTCGAAATCTGACCAACTTATTGGAATGTGAGTGGTAT
1561 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1620
V I A S Q A L S K S D Q L I G I
170 180
1621 TATCTGAATCTACGGATCTTCATTCTATTACAGAAATTATGATTCAATCGTTTGGCTCAA 1680
-----+-----+-----+-----+-----+-----+-----+-----+-----+
N Y D S I V W L K
190
1681 AGATAGTGGAACAGCTCCAAAATCTACATTGATTTATTTACGGATATTTTGCTGATGCT 1740
-----+-----+-----+-----+-----+-----+-----+-----+-----+
D S G T A P K S T F D L F T D I L L M L
200 210
A n1920/n2247
1741 AAAGTGAGTGAATAGAGTGCATGTAACATTTCAGCATGATTTTGAAATTATGAAAATTGGA 1800
-----+-----+-----+-----+-----+-----+-----+-----+-----+
K
CCTGGTTAGCTTTTAATTGATATTTTCGTGACGCTTGCATGTTTTGTGTGTTTGAAGACG
1801 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1860
AGCCCGTGTGTGAGCGACACGGATGACTCGCATTCGATCACCGACTTCATTAACCGTGT
1861 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1920
A n2273
1921 TCTTTCAAGAGCGAAGACGATCTTCTCAATTTCCCATCGGTGGAGCATGTCACGTCAGT 1980
-----+-----+-----+-----+-----+-----+-----+-----+-----+
S E D D L L N F P S V E H V T S V
220

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FIG. 1C

Intron 4

1981 TGTACTCAAAGGATGCTAAGTTGCTTGCCGATTCTGGTACAATATCTTAAATTATTGGT 2040
-----+-----+-----+-----+-----+-----+-----+
V L K R M

230
2041 TTTTAGATCTGCAACGCACTCATTGATCGTCCAAATACTTTATTTCGTATTTGATGACGTA 2100
-----+-----+-----+-----+-----+-----+-----+
I C N A L I D R P N T L F V F D D V
240 250

A n1948 T n1947

2101 GTTCAAGAAGAAACAATTTCGTTGGGCTCAGGAGCTACGTCTTCGATGTCTTGTAACACTACT 2160
-----+-----+-----+-----+-----+-----+-----+
V Q E E T I R W A Q E L R L R C L V T T
260 270

2161 CGTGACGTGGAAATATCAAATGCTGCTTCTCAAACATGCGAATTCATTGAAGTGACATCA 2220
-----+-----+-----+-----+-----+-----+-----+
R D V E I S N A A S Q T C E F I E V T S
280 290

2221 TTGGAATCGATGAATGTTATGATTTTCTAGAAGCTTATGGAATGCCGATGCCTGTTGGA 2280
-----+-----+-----+-----+-----+-----+-----+
L E I D E C Y D F L E A Y G M P M P V G
300 310

Tc4 n1416

2281 GAAAAAGAAGATGTGCTTAATAAAACAATCGAACTAAGCAGTGGAATCCAGCAACG 2340
-----+-----+-----+-----+-----+-----+-----+
E K E E D V L N K T I E L S S G N P A T
320 330

Intron 5

2341 CTTATGATGTTTTTCAAGTCTTGTGAACCGAAAACATTTGAAAAGTGAGTGGGACATACC 2400
-----+-----+-----+-----+-----+-----+-----+
L M M F F K S C E P K T F E K
330

2401 AATTTGAGACTTTTAAATAATTTATTCTACAATAAAAGTTAATCAAAAAGTTTCATAGC 2460
-----+-----+-----+-----+-----+-----+-----+
TGATTGTCTTTAAATTTTACGAATTGAGGATCAAAATCAAGAATTAGGATCCTGGCACGA
2461 -----+-----+-----+-----+-----+-----+-----+ 2520
GAGAAAACGTGTAGCTACCGTACCCGAGAGATTTTCTTGATATTTGCCATCGATTTAAT
2520 -----+-----+-----+-----+-----+-----+-----+ 2580
TTTTTAAGAAAATTATCGTTTACATAATTGAACAAGAGATACACGGTCTCGACCCGACG
2581 -----+-----+-----+-----+-----+-----+-----+ 2640
GAAATTTTAAATGAAAGCGAGTATGAGCCTGTTTTTCATTATTTTTTCGATTTTCTCTTG
2641 -----+-----+-----+-----+-----+-----+-----+ 2700
TTGTTTCTTTTATTTAAAGCCTTTTATTTTGAAAACAGTCTAAAAATATTAAAAACTGA
2701 -----+-----+-----+-----+-----+-----+-----+ 2760
ATAAAATATTTAAAAAATCAAGTAAATAGAAAAACAGCAAGGCTGGAGACTACTGTA
2760 -----+-----+-----+-----+-----+-----+-----+ 2820
CTTCTTAAATCCGCATACTCTTTTATTTAATCATTTTCCGGAATGTCGAAACGAAATAA
2821 -----+-----+-----+-----+-----+-----+-----+ 2880
TACATTTTGTAGTCCAAATCGCTAGGTATATTCTTAAATATCAAAACATTTTGCATTCA

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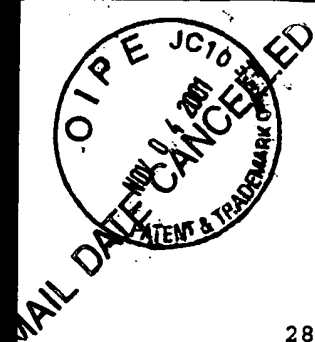
4/23
FIG. 1D

2881 +-----+-----+-----+-----+-----+-----+ 2940
GAATGGCACAGCTTAATAACAAATTGGAAAGTCGAGGATTAGTCGGTGTGAATGTATCA
2941 +-----+-----+-----+-----+-----+-----+ 3000
M A Q L N N K L E S R G L V G V E C I T
340 350
CCCCTTACTCGTACAAGTCACTCGCAATGGCTCTTCAAAGATGTGTTGAAGTTTTGTCAG
3001 +-----+-----+-----+-----+-----+-----+ 3060
P Y S Y K S L A M A L Q R C V E V L S D
360 370
ATGAGGATCGAAGTGCTCTTGCTTTTCGCAGTTGTGATGCCTCCTGGAGTTGATATACCCG
3061 +-----+-----+-----+-----+-----+-----+ 3120
E D R S A L A F A V V M P P G V D I P V
380 390
A n1894
↑
TCAAGCTATGGTCATGTGTTATTCCAGTTGATATTTGTTCAAATGAAGAAGAACAATTGG
3121 +-----+-----+-----+-----+-----+-----+ 3180
K L W S C V I P V D I C S N E E E Q L D
400 410
Intron 6
ATGATGAAGTTGCGGATCGGTTGAAAAGACTCAGCAAGTATGAGTCTTGAAATTTGAAGA
3181 +-----+-----+-----+-----+-----+-----+ 3240
D E V A D R L K R L S K
420
TTTAAATTAACACTTAAAATTTTCAGACGTGGAGCTCTTCTCAGTGGAAAACGAATGCCCCG
3241 +-----+-----+-----+-----+-----+-----+ 3300
R G A L L S G K R M P V
430 440
TTTTGACATTCAAAATTGATCATATTATCCATATGTTCTTGAAACACGTCGTTGATGCAC
3301 +-----+-----+-----+-----+-----+-----+ 3360
L T F K I D H I I H M F L K H V V D A Q
450 460
Intron 7
AAACTATCGCCGTATGCTGAAAATGTCTCAACTTTCAATTAAATTTTAAATTTTCAGAAAT
3361 +-----+-----+-----+-----+-----+-----+ 3420
T I A N
GGAATCTCAATTCTCGAGCAGCGTCTTCTTGAAATAGGAAACAATAATGTATCAGTACCG
3421 +-----+-----+-----+-----+-----+-----+ 3480
G I S I L E Q R L L E I G N N N V S V P
470 480
GAGCGACATATACCATCACATTTCCAAAAATTCGTCGTTTCATCAGCCAGTGAGATGTAT
3481 +-----+-----+-----+-----+-----+-----+ 3540
E R H I P S H F Q K F R R S S A S E M Y
500 510
CCAAAACTACAGAAGAACTGTGATCCGTCCTGAAGACTTCCCAAAGTTCATGCAATTG
3541 +-----+-----+-----+-----+-----+-----+ 3600
P K T T E E T V I R P E D F P K F M Q L
520 530
CACCAGAAATTCATGACTCCCTCAAAAATTTTGCATGCTGTTAAACCTATCGTGTACA
3601 +-----+-----+-----+-----+-----+-----+ 3660
H Q K F Y D S L K N F A C C *
540
ATATTGCCTGTATATTCCCCTCGAAATACGTTTATACTTTTTCGCACGAGTTTTCTCATT

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FIG. 1E

```
3661 -----+-----+-----+-----+-----+-----+ 3720
      TTTTCATTTGTACTTGTTTTATTTCTCTCCAAAATTTTCAGATCTATCCCAAATGTTCTTA
3721 -----+-----+-----+-----+-----+-----+ 3780
      AATTTAATGTTTTCTACAGATACTCAACACATCTTGTTTCATCTCATCCTTGCTTTTTTTT
3781 -----+-----+-----+-----+-----+-----+ 3840
      TTTCAAATATATTCAAGTTTCTTTTATAATTTTAATTAATCGAATTAATACATTACAGTAA
3841 -----+-----+-----+-----+-----+-----+ 3900
      AGAATTTTCGTGGACTATTATTTTATCGCATCCAAATGATTTATTCCCTATTGTTGAAAC
3901 -----+-----+-----+-----+-----+-----+ 3960
      TTCCAAATTGATCATTTTTTAAACACGCCTCATTAAATTGAAAGTCGTACTTTTAGTCTCG
3961 -----+-----+-----+-----+-----+-----+ 4020
      AACATGAAGTAAGTTATTTTCTGTGTTCTAAATTCAAAGTGCATTCCAAAAGGACATTTG
4021 -----+-----+-----+-----+-----+-----+ 4080
      ATGAGTTTTTCACGAAAACCGTAATTTTACAATTTCTTTTCAGTTTTGAAGATGTTGAT
4081 -----+-----+-----+-----+-----+-----+ 4140
      TTCTTTCTCTGTTGGCGTCATTACTACATTTGCTTTGCTGCTTCACTTTATCGAGATTC
4141 -----+-----+-----+-----+-----+-----+ 4200
      TTGCCATCAATGGAGTTCCATCTAGACCGATAGCAGTCTTCATATCATTATCCCTGTATA
4201 -----+-----+-----+-----+-----+-----+ 4260
      TTGTACTGTTTCAGTATTTTAACTTATCGATTACGTACTATATTCAAGTGGTTCACTGTTT
4261 -----+-----+-----+-----+-----+-----+ 4320
      TCGGTCAATGGGTGACACGTGCTCGACGANNAATTTTCAACGAACGCAATCTCCTAGTCA
4320 -----+-----+-----+-----+-----+-----+ 4380
      CTTATCAACCAAGAGCCCTCACCCATG
4380 -----+-----+-----+-----+-----+-----+ 4407
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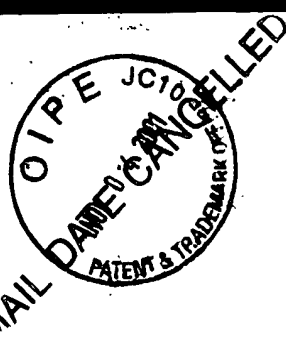
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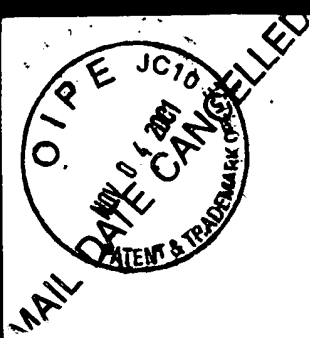
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FIG. 2





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FIG. 3

	10	12	14	18	21
	X	Y	Z	-X	-Z
	D	N	S	T	E
Calcium-binding loop consensus		D	N	S	
			D	E	
				Q	
				D	
				N	
EF-hand consensus	<u>O * O * O G * * O * * E</u>				
ced-4 sequence 1	<u>Y</u> <u>N</u> <u>N</u> <u>Q</u> <u>S</u> <u>H</u> <u>L</u> <u>A</u> <u>D</u> <u>F</u> <u>L</u> <u>E</u>				
sequence 2	<u>S</u> <u>L</u> <u>E</u> <u>I</u> <u>D</u> <u>E</u> <u>C</u> <u>Y</u> <u>D</u> <u>F</u> <u>L</u> <u>E</u>				
Parvalbumin (carp)	D Q D K S G F I <u>E</u> E D E				
(hake)	D Q D K D <u>D</u> F I <u>G</u> E D E				
(ray)	D S D G D <u>H</u> K I <u>G</u> V D E				
SCBP (<i>Amphioxus I</i>)	D I N K D <u>D</u> V V S W E E				
ICaBP (bovine)	A K <u>E</u> G D <u>P</u> Q L S K E E				
	D K N G D <u>G</u> E V S F E E				
Troponin C (rabbit)	D A D G <u>G</u> <u>G</u> D I S V K E				
	D E D G <u>S</u> <u>G</u> T I D F E E				
	D R N A D G Y I D A E E				
	D K N N D G R I D F D E				
Calmodulin (bovine)	D K D G N G T I T T K E				
Trypsinogen	<u>L</u> <u>G</u> <u>E</u> D N <u>I</u> N V V E G N E				
Fibrinogen	D N D N D <u>K</u> F E G N C A <u>E</u>				
Villin	<u>G</u> V D P S <u>R</u> K E N H L S				
GBP	D L N K D G Q I Q <u>I</u> E				

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FIG. 4A

ced-3 Genomic Sequence

AGATCTGAAATAAGGTGATAAATTAATAAATTAAGTGTATTTCTGAGGAAATTTGACTGT
1 -----+-----+-----+-----+-----+-----+-----+ 60
TTTAGCACAAATTAATCTTGTTCAGAAAAAGTCCAGTTTCTAGATTTTCCGTCTTA
61 -----+-----+-----+-----+-----+-----+-----+ 120
TTGTCGAATTAATATCCCTATTATCACTTTTTCATGCTCATCCTCGAGCGGCACGTCTC
121 -----+-----+-----+-----+-----+-----+-----+ 180
AAAGAATTGTGAGAGCAAACGCGCTCCCATGACCTCCACACTCAGCCGCCAAAACAAAC
181 -----+-----+-----+-----+-----+-----+-----+ 240
GTTCGAACATTCGTGTGTGTGCTCCTTTTCCGTTATCTTGCAGTCATCTTTGTCGTTT
241 -----+-----+-----+-----+-----+-----+-----+ 300
TTTTCTTTGTTCTTTTTGTTGAACGTGTTGCTAAGCAATTATTACATCAATTGAAGAAAA
301 -----+-----+-----+-----+-----+-----+-----+ 360
GGCTCGCCGATTTATTGTTGCCAGAAAGATTCTGAGATTCTCGAAGTCGATTTTATAATA
361 -----+-----+-----+-----+-----+-----+-----+ 420
TTTAACCTTGGTTTTTGCATTGTTTCGTTTAAAAAAACCACTGTTTATGTGAAAAACGAT
421 -----+-----+-----+-----+-----+-----+-----+ 480
TAGTTTACTAATAAAACTACTTTTAAACCTTTACCTTTACCTCACCGCTCCGTGTTTCATG
481 -----+-----+-----+-----+-----+-----+-----+ 540
GCTCATAGATTTTTCGATACTCAAATCCAAAAATAAATTTACGAGGGCAATTAATGTGAAA
541 -----+-----+-----+-----+-----+-----+-----+ 600
CAAAAAACAATCCTAAGATTTCCACATGTTTGACCTCTCCGGCACCTTCTTCCCTTAGCCCC
601 -----+-----+-----+-----+-----+-----+-----+ 660
ACCACTCCATCACCTCTTTGGCGGTGTTCTTCGAAACCACTTAGGAAAGCAGTGTGTAT
661 -----+-----+-----+-----+-----+-----+-----+ 720
CTCATTTGGTATGCTCTTTTCGATTTTATAGCTCTTTGTGCGCAATTTCAATGCTTTAAAC
721 -----+-----+-----+-----+-----+-----+-----+ 780
AATCCAAATCGCATTATATTTGTGCATGGAGGCAAATGACGGGGTTGGAATCTTAGATGA
781 -----+-----+-----+-----+-----+-----+-----+ 840
GATCAGGAGCTTTCAGGGTAAACGCCCGGTTTCAATTTGTACCACATTTTCATCATTTTCCT
841 -----+-----+-----+-----+-----+-----+-----+ 900
GTCGTCCTTGGTATCCTCAACTTGTCCCGGTTTTGTTTTCGGTACACTCTTCCGTGATGC
901 -----+-----+-----+-----+-----+-----+-----+ 960
CACCTGTCTCCGTCTCAATTATCGTTTAAAGATGTGAACTGTCCAGATGGGTGACTCATA
961 -----+-----+-----+-----+-----+-----+-----+ 1020
TTGCTGCTGCTACAATCCACTTTCTTTTCTCATCGGCAGTCTTACGAGCCCATCATAAAC
1021 -----+-----+-----+-----+-----+-----+-----+ 1080
TTTTTTTTCCGCGAAATTTGCAATAAACCGGCCAAAAACTTTCTCAAATTGTTACGCAA
1081 -----+-----+-----+-----+-----+-----+-----+ 1140
TATATACAATCCATAAGAATATCTTCTCAATGTTTATGATTTCTTCGAGCACTTTCTCT
1141 -----+-----+-----+-----+-----+-----+-----+ 1200
TCGTGTGCTAACATCTTATTTTATAATATTTCCGCTAAAATTCCGATTTTGTAGTATTA
1201 -----+-----+-----+-----+-----+-----+-----+ 1260
ATTTATCGTAAAATTATCATAATAGCACCAGAAACTACTAAAAATGGTAAAAGCTCCTTT
1261 -----+-----+-----+-----+-----+-----+-----+ 1320

Repeat 1
TAAATCGGCTCGACATTATCGTATTAAGGAATCACAAAATTCTGAGAATGCGTACTGCGC
1321 -----+-----+-----+-----+-----+-----+-----+ 1380

AACATATTTGACGGCAAATATCTCGTAGCGAAACTACAGTAATCTTTAAATGACTAC
1381 -----+-----+-----+-----+-----+-----+-----+ 1440

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FIG. 4B

-----> Repeat 1
TGTAGCGCTTGTGTCGATTTACGGGCTCAATTTTTGAAAATAATTTTTTTTTTCGAATTT
1441 -----+-----+-----+-----+-----+-----+ 1500

TGATAACCCGTAAATCGTCAACGCTACAGTAGTCATTTAAAGGATTACTGTAGTTCTA
1501 -----+-----+-----+-----+-----+-----+ 1560

GCTACGAGATATTTTGC GCGCCAAATATGACTGTAATACGCATTCTCTGAATTTTGTGTT
1561 -----+-----+-----+-----+-----+-----+ 1620
TCCGTAATAATTTTCAAGATTTTGGCATTCCACTTTAAAGGCGCACAGGATTTATTCCA
1621 -----+-----+-----+-----+-----+-----+ 1680
ATGGGTCTCGGCACGCAAAAAGTTTGATAGACTTTTAAATTCTCCTTGCAATTTTAAATC
1681 -----+-----+-----+-----+-----+-----+ 1740
AATTACTAAAATTTTCGTGAATTTTCTGTTAAAATTTTAAAATCAGTTTCTAATATT
1741 -----+-----+-----+-----+-----+-----+ 1800
TTCCAGGCTGACAAACAGAAACAAAAACACAACAAACATTTTAAAATCAGTTTCAAAT
1801 -----+-----+-----+-----+-----+-----+ 1860
TAAAAATAACGATTTCTCATTGAAAATTGTGTTTTATGTTTGC GAAAAATAAAAGAGAACT
1861 -----+-----+-----+-----+-----+-----+ 1920
GATTCAAAACAATTTTAACAAAAAAAAAACCCCAAAATTCGCCAGAAATCAAGATAAAAAA
1921 -----+-----+-----+-----+-----+-----+ 1980
TTCAAGAGGGTCAAAATTTTCCGATTTTACTGACTTTCACCTTTTTTTTCGTAGTTCAGT
1981 -----+-----+-----+-----+-----+-----+ 2040
GCAGTTGTTGGAGTTTTTACGAAAACTAGGAAAAAAATCGATAAAATTAATCAATCG
2041 -----+-----+-----+-----+-----+-----+ 2100
AGCTGAATTTTGAGGACAATGTTTAAAAAAAACACTATTTTCCAATAATTTCACTCAT
2101 -----+-----+-----+-----+-----+-----+ 2160

TTTCAGACTAAATCGAAAAATCAAAATCGTACTCTGACTACGGGTCAGTAGAGAGGTCAACC

2161 -----+-----+-----+-----+-----+-----+ 2220

ATCAGCCGAAGATGATGCGTCAAGATAGAAGGAGCTTGCTAGAGAGGAACATTATGATGT
2221 -----+-----+-----+-----+-----+-----+ 2280
M M R Q D R R S L L E R N I M M F
1 10
T (n1040)
|
TCTCTAGTCATCTAAAAGTCGATGAAATTCTCGAAGTTCTCATCGCAAAACAAGTGTGA
2281 -----+-----+-----+-----+-----+-----+ 2340
S S H L K V D E I L E V L I A K Q V L N
20 30
| Intron 1
ATAGTGATAATGGAGATATGATTAATGTGAGTTTTTAATCGAATAATAATTTTAAAAAAA
2341 -----+-----+-----+-----+-----+-----+ 2400
S D N G D M I N
40

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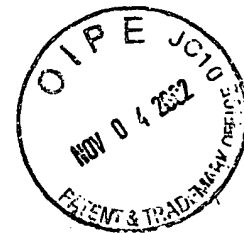
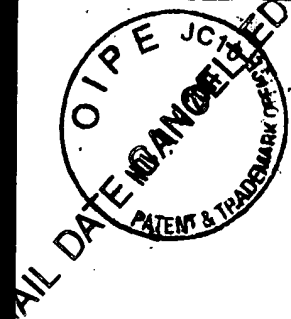
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FIG. 4C

AATTGATAATATAAAGAATATTTTTGCAGTCATGTGGAACGGTTCGCGAGAAGAGACGGG
2401 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 2460
S C G T V R E K R R E
50
A (n718)
AGATCGTGAAAGCAGTGCAACGACGGGGAGATGTGGCGTTCGACGCGTTTTATGATGCTC
2461 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2520
I V K A V Q R R G D V A F D A F Y D A L
60 70
| Intron 2
TTCGCTCTACGGGACACGAAGGACTTGCTGAAGTTCTTGAACCTCTCGCCAGATCGTAGG
2521 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2580
R S T G H E G L A E V L E P L A R S
80 90
TTTTTAAAGTTTCGGCGCAAAAGCAAGGGTCTCACGAAAAAAGAGGCGGATCGTAATTTT
2581 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2640
GCAACCCACCGGCACGGTTTTTTTCTCCGAAAATCGGAAATTATGCACTTTCCCAAATAT
2641 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2700
TTGAAGTGAAATATATTTTATTTACTGAAAGCTCGAGTGATTATTTATTTTTTAACACTA
2701 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2760
ATTTTCGTGGCGCAAAAGGCCATTTTGTAGATTTGCCGAAAATACTTGTCACACACACAC
2761 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2820
ACACACATCTCCTTCAAATATCCCTTTTTCCAGTGTTGACTCGAATGCTGTGCAATTCGA
2821 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2880
V D S N A V E F E
100
GTGTCCAATGTACACGGCAAGCCATCGTCGGAGCCGCGCATTGAGCCCCGCCGGCTACAC
2881 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2940
C P M S P A S H R R S R A L S P A G Y T
110 120
TTCACCGACCCGAGTTCACCGTGACAGCGTCTCTTCAGTGTGTCATTCATTCTTTATCA
2941 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3000
S P T R V H R D S V S S V S S F T S Y Q
130 140
GGATATCTACTCAAGAGCAAGATCTCGTTCTCGATCGCGTGCACTTCATTTCATCGGATCG
3001 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3060
D I Y S R A R S R S R S R A L H S S D R
150 160
| Intron 3
ACACAATTATTCATCTCCTCCAGTCAACGCATTTCCAGCCAACCTTGATGTTGATGCG
3061 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3120
H N Y S S P P V N A F P S Q P S
170



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FIG. 4D

Repeat 1

AACACTAAATTCTGAGAATGCGCATTACTCAACATATTTGACGCGCAAATATCTCGTAGC
3121 -----+-----+-----+-----+-----+-----+ 3180

GAAAAATACAGTAACCCCTTTAAATGACTATTGTAGTGTGCGATTACGGGCTCGATTTTCG
3181 -----+-----+-----+-----+-----+-----+ 3240
-->
AAACGAATATATGCTCGAATTGTGACAACGAATTTTAATTTGTCATTTTTGTGTTTTCTT
3241 -----+-----+-----+-----+-----+-----+ 3300

Repeat 1

<-----
TTGATATTTTTGATCAATTAATAAATTATTTCCGTAAACAGACACCAGCGCTACAGTACT
3301 -----+-----+-----+-----+-----+-----+ 3360

CTTTTAAAGAGTTACAGTAGTTTTCGCTTCAAGATATTTTGAAAAGAATTTTAAACATTT
3361 -----+-----+-----+-----+-----+-----+ 3420
TGAAAAAAAATCATCTAACATGTGCCAAAACGCTTTTTTCAAGTTTCGCAGATTTTTTGA
3421 -----+-----+-----+-----+-----+-----+ 3480

Repeat 2

TTTTTTTTCATTCAAGATATGCTTATTAACACATATAATTATCATTAAATGTGAATTTCTTG
3481 -----+-----+-----+-----+-----+-----+ 3540

TAGAAATTTTGGGCTTTTCGTTCTAGTATGCTCTACTTTTGAAATTGCTCAACGAAAAAA
3541 -----+-----+-----+-----+-----+-----+ 3600

TCATGTGGTTTGTTCATATGAATGACGAAAAATAGCAATTTTTTATATATTTTCCCCTAT
3601 -----+-----+-----+-----+-----+-----+ 3660

TCATGTTGTGCAGAAAAATAGTAAAAAAGCGCATGCATTTTTCGACATTTTTTACATCGA
3661 -----+-----+-----+-----+-----+-----+ 3720
----->
ACGACAGCTCACTTCACATGCTGAAGACGAGAGACGCGGAGAAATACCACACATCTTTCT
3721 -----+-----+-----+-----+-----+-----+ 3780

Repeat 2
<-----
GCGTCTCTCGTCTTCAGCATGTGAAATGGGATCTCGGTCGATGTAAAAAATGTGAATA
3781 -----+-----+-----+-----+-----+-----+ 3840

ATGTAAAAAATGCATGCGTTTTTTTTACACTTTTCTGCACAAATGAATAGGGGGAAAAATGT
3841 -----+-----+-----+-----+-----+-----+ 3900

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Filing Date: May 24, 2000 Serial No.: 09/577,897
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FIG. 4E

```
-----
ATTAAAATACATTTTTTGTATTTTCAACATCACATGATTAACCCCATTTATTTTTTCGTT
3901 -----+-----+-----+-----+-----+-----+ 3960

-----
GAGCAACTTAAAAAGTAGAGAATATTAGAGCGAAAACCAAATTTCTTCAAGATATTACC
3961 -----+-----+-----+-----+-----+-----+ 4020

-----
TTTATTGATAATTATAGATGTTAATAAGCATATCTTGAATGAAAGTCAGCAAAAATATGT
4021 -----+-----+-----+-----+-----+-----+ 4080
GCGAAACACCTGAAAAAATCAAAAATTCTGCGAAAATTGAAAAATGCATTAAATACA
4081 -----+-----+-----+-----+-----+-----+ 4140
TTTTTGCATTTTTCTACATCACATGAATGTAGAAAATTAAAAGGGAAATCAAAATTTCTA
4141 -----+-----+-----+-----+-----+-----+ 4200
GAGGATATAATTGAATGAAACATTGCGAAAATTAAAATGTGCGAAACGTCAAAAAAGAGGA
4201 -----+-----+-----+-----+-----+-----+ 4260

AATTTGGGTATCAAAATCGATCCTAAAACCAACACATTTTCAGCATCCGCCAACTCTTCAT
4261 -----+-----+-----+-----+-----+-----+ 4320
                                     S A N S S F
                                     180

TCACCGGATGCTCTTCTCTCGGATACAGTTCAAGTCGTAATCGCTCATTTCAGCAAAGCTT
4321 -----+-----+-----+-----+-----+-----+ 4380
    T G C S S L G Y S S S R N R S F S K A S
    190                                200

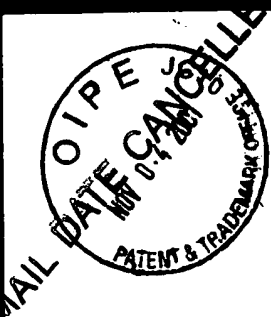
CTGGACCAACTCAATACATATTCCATGAAGAGGATATGAACTTTGTCGATGCACCAACCA
4380 -----+-----+-----+-----+-----+-----+ 4440
    G P T Q Y I F H E E D M N F V D A P T I
    210                                220

TAAGCCGTGTTTTTCGACGAGAAAAACCATGTACAGAACTTCTCGAGTCCTCGTGGAATGT
4441 -----+-----+-----+-----+-----+-----+ 4500
    S R V F D E K T M Y R N F S S P R G M C
    230                                240

GCCTCATCATAAATAATGAACACTTTGAGCAGATGCCAACACGGAATGGTACCAAGGCCG
4501 -----+-----+-----+-----+-----+-----+ 4560
    L I I N N E H F E Q M P T R N G T K A D
    250                                260

ACAAGGACAATCTTACCAATTTGTTTCAGATGCATGGGCTATACGGTTATTTGCAAGGACA
4561 -----+-----+-----+-----+-----+-----+ 4620
    K D N L T N L F R C M G Y T V I C K D N
    270                                280

| Intron 4
ATCTGACGGGAAGGGTACGGCGAAATTATATTACCCAAACGCGAAATTTGCCATTTTGCG
4621 -----+-----+-----+-----+-----+-----+ 4680
    L T G R
```



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FIG. 4F

Repeat 3

----->
CCGAAAATGTGGCGCCCGGTCTCGACACGACAATTTGTGTAAATGCAAAAATGTATAAT
4681 -----+-----+-----+-----+-----+-----+-----+ 4740
TTTGCAAAAAACAAAATTTTGAACCTCCGCGAAAATGATTTACCTAGTTTCGAAATTTTC
4741 -----+-----+-----+-----+-----+-----+-----+ 4800
GTTTTTTCGGCTACATTATGTGTTTTTTCTTAGTTTTTCTATAATATTTGATGTAAAA
4801 -----+-----+-----+-----+-----+-----+-----+ 4860
ACCGTTTGTAAATTTTCAGACAATTTTCCGCATACAAAACCTTGATAGCACGAAATCAATT
4861 -----+-----+-----+-----+-----+-----+-----+ 4920
TTCTGAATTTTCAAAATTATCCAAAATGCACAATTTAAAATTTGTGAAAATTGGCAAAC
4921 -----+-----+-----+-----+-----+-----+-----+ 4980
GGTGTTCATATGAAATGTATTTTTTAAAACTTTAAAAACCACTCCGAAAAGCAATAA
4981 -----+-----+-----+-----+-----+-----+-----+ 5040
AAATCAAAAACACGTCACAATTCAAATTCAAAAGTTATTCATCCGATTTGTTTATTTTTG
5041 -----+-----+-----+-----+-----+-----+-----+ 5100
CAAAATTTGAAAAAATCATGAAGGATTTAGAAAAGTTTTATAACATTTTTTCTAGATTTT
5101 -----+-----+-----+-----+-----+-----+-----+ 5160
TCAAAATTTTTTTTAAACAAATCGAGAAAAAGAGAATGAAAAATCGATTTTAAAAATATCC
5161 -----+-----+-----+-----+-----+-----+-----+ 5220

Repeat 3

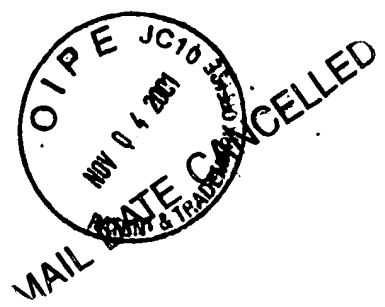
<-----
ACAGCTTCGAGAGTTTGAAATTACAGTACTCCTTAAAGGCGCACACCCCATTTGCATTGG
5221 -----+-----+-----+-----+-----+-----+-----+ 5280

ACCAAAAATTTGTCGTGTCGAGACCAGGTACCGTAGTTTTTGTGCGAAAAATTGCACCAT
5281 -----+-----+-----+-----+-----+-----+-----+ 5340
TGGACAATAAACCTTCCTAATCACAAAAAGTAAATTTGAAATCTTCGAAAAGCCAAAAA
5341 -----+-----+-----+-----+-----+-----+-----+ 5400
ATTCAAAAAAAGTCGAATTTTCGATTTTTTTTTTGGTTTTTTGGTCCCAAAAACCAAAA
5401 -----+-----+-----+-----+-----+-----+-----+ 5460
AAATCAATTTTCTGCAAAATACCAAAAAAGAAACCCGAAAAAATTTCCAGCCTTGTTCT
5461 -----+-----+-----+-----+-----+-----+-----+ 5520

|
AATGTAAACTGATATTTAATTTCCAGGGAATGCTCCTGACAATTCGAGACTTTGCCAAAC
5521 -----+-----+-----+-----+-----+-----+-----+ 5580
G M L L T I R D F A K H
290 300

ACGAATCACACGGAGATTCTGCGATACTCGTGATTCTATCACACGGAGAAGAGAATGTGA
5581 -----+-----+-----+-----+-----+-----+-----+ 5640
E S H G D S A I L V I L S H G E E N V I
310 320

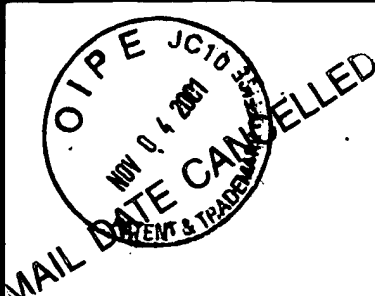
TTATTGGAGTTGATGATATACCGATTAGTACACAGAGATATATGATCTTCTCAACGCGG
5641 -----+-----+-----+-----+-----+-----+-----+ 5700
I G V D D I P I S T H E I Y D L L N A A
330 340



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FIG. 4G

A (n2433)
| Intron 5
CAAATGCTCCCCGTCTGGCGAATAAGCCGAAAATCGTTTTTGTGCAGGCTTGTTCGAGGCG
5701 -----+-----+-----+-----+-----+-----+-----+ 5760
N A P R L A N K P K I V F V Q A C R G E
350 360
|
GTTCGTTTTTTTATTTTAAATTTTAAATATAAATATTTTAAATAAATTCATTTTCAGAACGTC
5761 -----+-----+-----+-----+-----+-----+-----+ 5820
R R
|
GTGACAATGGATTCCCAGTCTTGGATTCTGTGCGACGGAGTTTCCTGCATTTCTTCGTCGTG
5821 -----+-----+-----+-----+-----+-----+-----+ 5880
D N G F P V L D S V D G V P A F L R R G
370 380
T (n1165)
|
GATGGGACAATCGAGACGGGCCATTGTTCAATTTTCTTGGATGTGTGCGGCCGCAAGTTC
5881 -----+-----+-----+-----+-----+-----+-----+ 5940
W D N R D G P L F N F L G C V R P Q V Q
390 400
| Intron 6
AGGTTGCAATTTAATTTCTTGAATGAGAATATTCCTTCAAAAAATCTAAAATAGATTTTT
5941 -----+-----+-----+-----+-----+-----+-----+ 6000
ATTCCAGAAAGTCCCGATCGAAAAATTGCGATATAATTACGAAATTTGTGATAAAATGAC
6001 -----+-----+-----+-----+-----+-----+-----+ 6060
Repeat 4

AAACCAATCAGCATCGTCGATCTCCGCCCACTTCATCGGATTGGTTTGAAAGTGGGCGGA
6061 -----+-----+-----+-----+-----+-----+-----+ 6120
----->
GTGAATTGCTGATTGGTCGCAGTTTTTCAGTTTAGAGGGAATTTAAAAATCGCCTTTTCGA
6121 -----+-----+-----+-----+-----+-----+-----+ 6180
AAATTAAAAATTGATTTTTTCAATTTTTTCGAAAAATATTCCGATTATTTTATATTCTTT
6181 -----+-----+-----+-----+-----+-----+-----+ 6240
A (n717)
|
GGAGCGAAAGCCCCGTCTGTAAACATTTTTAAATGATAATTAATAAAATTTTGCAGCAA
6241 -----+-----+-----+-----+-----+-----+-----+ 6300
Q
T (n1949)
|
GTGTGGAGAAAGAAGCCGAGCCAAGCTGACATTCTGATTGATACGCAACGACAGCTCAA
6301 -----+-----+-----+-----+-----+-----+-----+ 6360
V W R K K P S Q A D I L I R Y A T T A Q
410 420



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FIG. 4H

A (n1286)
|
TATGTTTCGTGGAGAAACAGTGCTCGTGGATCATGGTTCATTCAAGCCGTCTGTGAAGTG
6361 -----+-----+-----+-----+-----+ 6420
Y V S W R N S A R G S W F I Q A V C E V
430 440

T (n1129, n1164)
|
TTCTCGACACACGCAAAGGATATGGATGTTGTTGAGCTGCTGACTGAAGTCAATAAGAAG
6421 -----+-----+-----+-----+-----+ 6480
F S T H A K D M D V V E L L T E V N K K
450 460

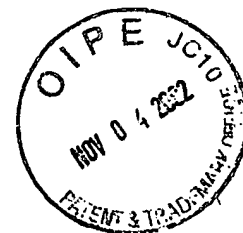
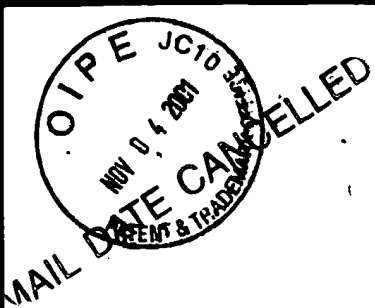
T (n2430) A (n2426)
| | Intron 7
GTCGCTTGTGGATTTCAGACATCACAGGGATCGAATATTTTGAAACAGATGCCAGAGGTA
6481 -----+-----+-----+-----+-----+ 6540
V A C G F Q T S Q G S N I L K Q M P E
470 480

Repeat 5

CTTGAAACAAACAATGCATGTCTAACTTTTAAAGGACACAGAAAAATAGGCAGAGGCTCCT
6541 -----+-----+-----+-----+-----+ 6600
----->
TTTGCAAGCCTGCCGCGCGTCAACCTAGAAATTTTAGTTTTCTAGCTAAAATGATTGATTTT
6601 -----+-----+-----+-----+-----+ 6660
GAATATTTTATGCTAATTTTTTTCGTTAAATTTTGAAATAGTCACTATTATCGGGTTT
6661 -----+-----+-----+-----+-----+ 6720
CCAGTAAAAAATGTTTATTAGCCATTGGATTTTACTGAAAAACGAAAATTTGTAGTTTTTC
6721 -----+-----+-----+-----+-----+ 6780
AACGAAATTTATCGATTTTAAATGTAAAAAATAAGCGAAAAATTACATCAACCATCAA
6781 -----+-----+-----+-----+-----+ 6840
GCATTTAAGCCAAAATTGTAACTCATTTAAAAATTAATTCAAAGTTGTCCACGAGTATT
6841 -----+-----+-----+-----+-----+ 6900

Repeat 5
-----<
ACACGGTTGGCGCGCGCAAGTTTGCAAAACGACGCTCCGCTCTTTTTCTGTGCGGCTT
6901 -----+-----+-----+-----+-----+ 6960

T (n1163)
| |
GAAAACAAGGGATCGGTTTAGATTTTTCCCAAAATTTAAATTAAATTTTCAGATGACATC
6961 -----+-----+-----+-----+-----+ 7020
M T S
CCGCCTGCTCAAAAAGTTCTACTTTTGGCCGGAAGCACGAAACTCTGCCGTCTAAAATTC
7021 -----+-----+-----+-----+-----+ 7080
R L L K K F Y F W P E A R N S A V *
490 500



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FIG. 4I

ACTCGTGATTCATTGCCCAATTGATAATTGTCTGTATCTTCTCCCCAGTTCTCTTTTCGC
7081 -----+-----+-----+-----+-----+ 7140
CCAATTAGTTTAAAACCATGTGTATATTGTTATCCTATACTCATTTCACCTTTATCATTCT
7141 -----+-----+-----+-----+-----+ 7200
ATCATTCTCTTCCCATTTTCACACATTTCCATTTCTCTACGATAATCTAAAATTATGAC
7201 -----+-----+-----+-----+-----+ 7260
GTTTGTGTCTCGAACGCATAATAATTTTAATAACTCGTTTTGAATTTGATTAGTTGTTGT
7261 -----+-----+-----+-----+-----+ 7320
GCCCAGTATATATGTATGTACTATGCTTCTATCAACAAAATAGTTTCATAGATCATCACC
7321 -----+-----+-----+-----+-----+ 7380
CCAACCCACCAACCTACCGTACCATATTCATTTTTGCCGGAATCAATTCGATTAATT
7381 -----+-----+-----+-----+-----+ 7440
TTAACCTATTTTTTCGCCACAAAAAATCTAATATTTGAATTAACGAATAGCATTCCCATC
7441 -----+-----+-----+-----+-----+ 7500
TCTCCCGTGCCGGAATGCCTCCCGGCCTTTTAAAGTTTCGGAACATTTGGCAATTATGTAT
7501 -----+-----+-----+-----+-----+ 7560
AAATTTGTAGGTCCCCCATCATTTCCCGCCCATCATCTCAAATTGCATTCTTTTTTCG
7561 -----+-----+-----+-----+-----+ 7620
CCGTGATATCCCGATTCTGGTCAGCAAAGATCT
7621 -----+-----+-----+-----+ 7653

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11/11-34
10/10-34

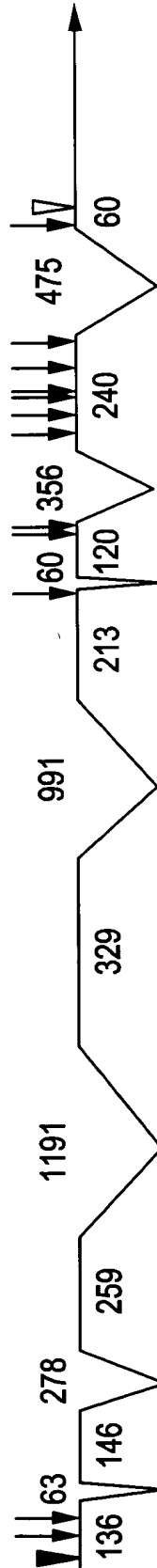
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NOV 04 2001
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Title: CLONING, SEQUENCING, AND CHARACTERIZATION
OF TWO CELL DEATH GENES AND USES THEREFOR
Applicant(s): H. Robert Horvitz et al.
Filing Date: May 24, 2000 Serial No.: 09/577,897
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FIG. 5A



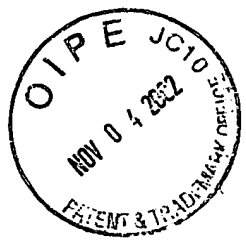
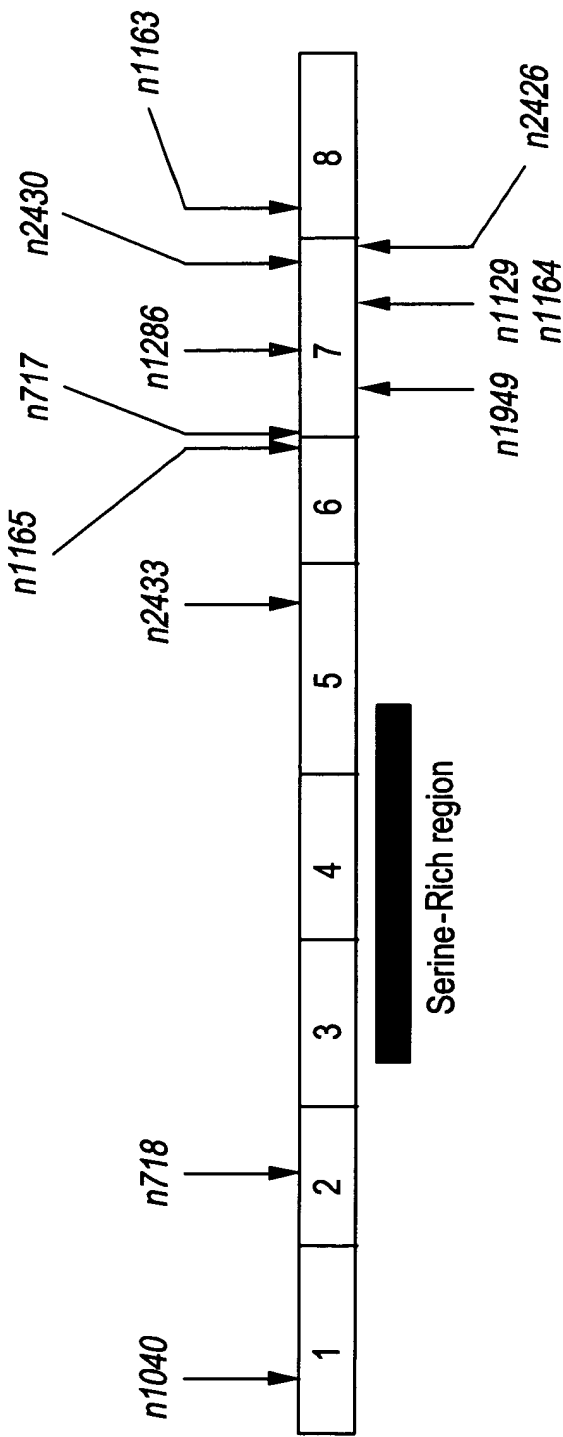


FIG. 5B

ced-3 Mutations are Clustered



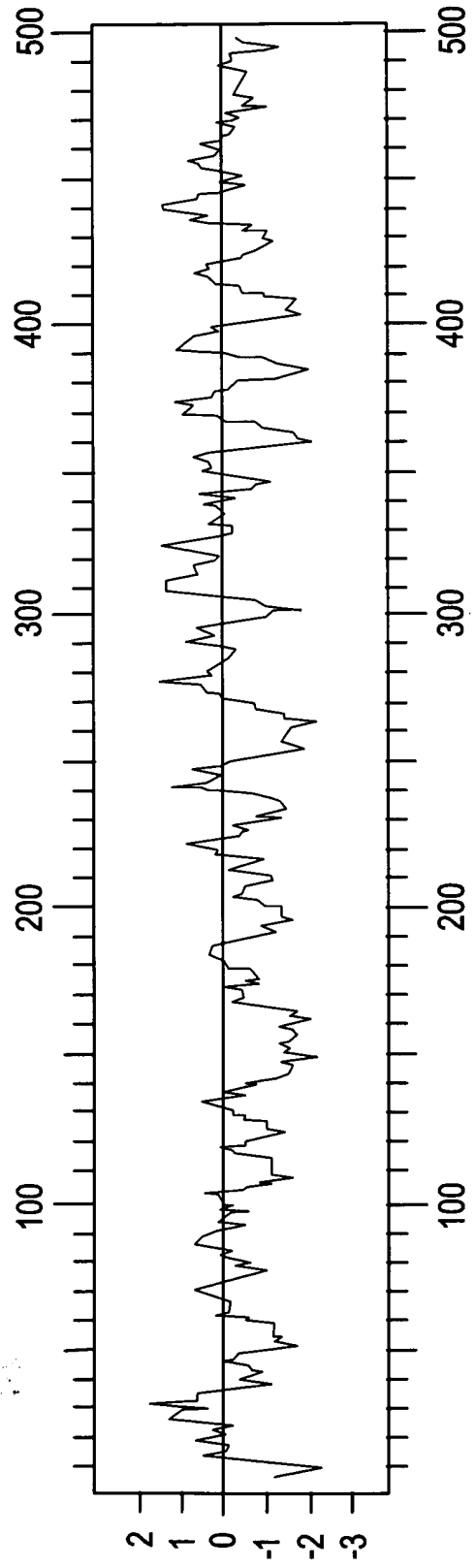
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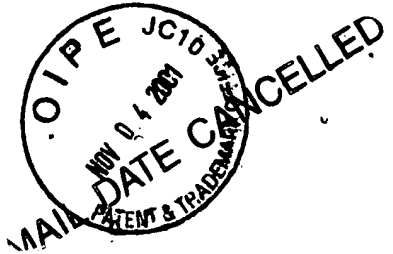
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Filing Date: May 24, 2000 Serial No.: 09/577,897
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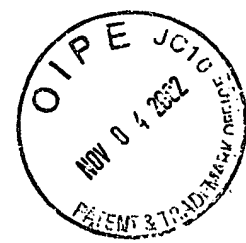
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FIG. 6





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Filing Date: May 24, 2000 Serial No.: 09/577,897
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FIG. 7

Lines

```
1 01 MMRQDRRSLLERNIMMFSSHLKVDEILEVLIAKQVLNSDNGDMINSCGTV 50
2 .....W.....LE...K.QA.L..D.....V....R.E
3 TVS.SLI..R..... M.....

1 51 REKRREIVKAVQRPQDVAFDADFALRSTGHEGLAEVLEPLARSVDSNAV 100
2 .DNEK.....R..E.....D...ND..D..M..S.P .P.
3

1 101 EFECPMSPASHRRSRALSPAGYTSPTVRHRSVSSVSSFTS_YQDIYSRA 149
2 PM.....S.....P .A.....I.....T...V....
3 S

1 150 RSRSR_SRALHSSDRHNYSSPPVNAFSPQSSANSSTGCSLLGYSSSRN 198
2 ..S..S..P.Q.....M.AA_TS.....A.....
3 T...__..P..T.....V..S..S.Q...A.....S.....T

1 199 RSFSKASGPTQYIFHEEDMNFVDAPTISR VFDEKTM YRNFSSPRGMCLI 247
2 .....T.AQS.....Y.....H.....L...
3 ..Y....AHS.....Y.....H.....T...L...

1 248 INNEHFQMPTRNGTKADKDNLTNLFRCMGYTVICKDNLTGRGMLLTIRD 297
2 .....I.....E..S...S
3 .....P....IS.....I.H.....M.....

1 298 FAKHESHGDSAILVILSHGEENVIIGVDDIPISTHEIYDLLNAANAPRLA 347
2 .GRNDM.....VSVNV.....
3 ...N.T.....VSVNV....X.....

1 348 NKP KIVFVQACRGERRDNGFPVLDSVDGVP AFLRRGWDNRDGPLFNFLGC 397
2 ....L.....SLI.....
3 ....L.....V.....LI....KG....

1 398 VRPQVQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFIQAVCEVFST 447
2 .....M..A.....L
3 ....A.....A.....L

1 448 HAKMDVVELLTEVNKKVACGFQTSQGSNILKQMPMTSRL LKKFYFWPE 497
2 .....L.....
3 .....A.....L.....

1 498 __ARN__ SAV 503
2 DRG..__...
3 __D..RS...
```

Line 1 c. *elegans*
Line 2 c. *briggsae*
Line 3 c. *vulgaris*

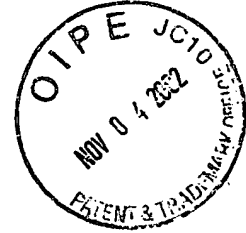
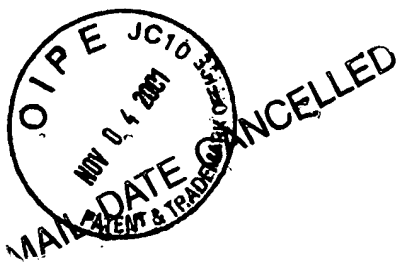
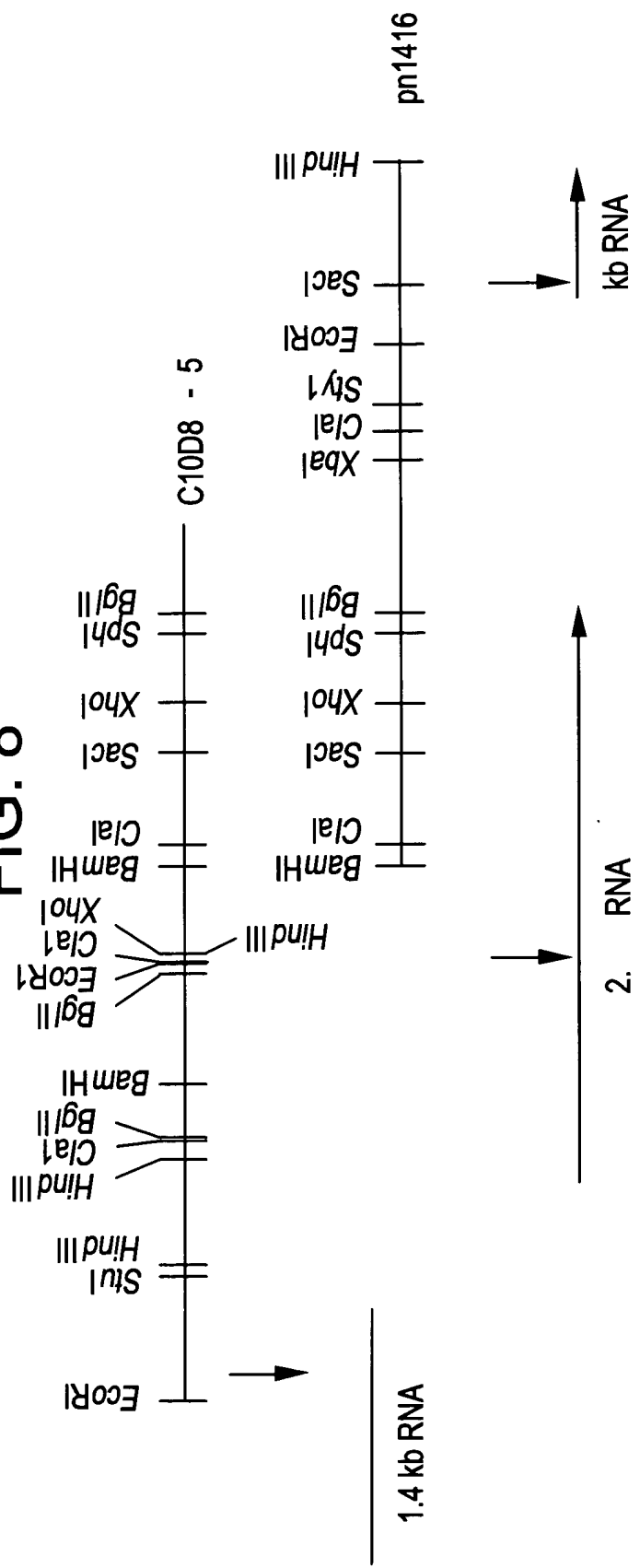
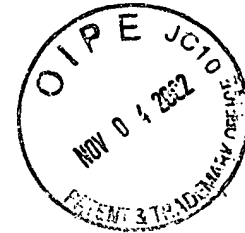


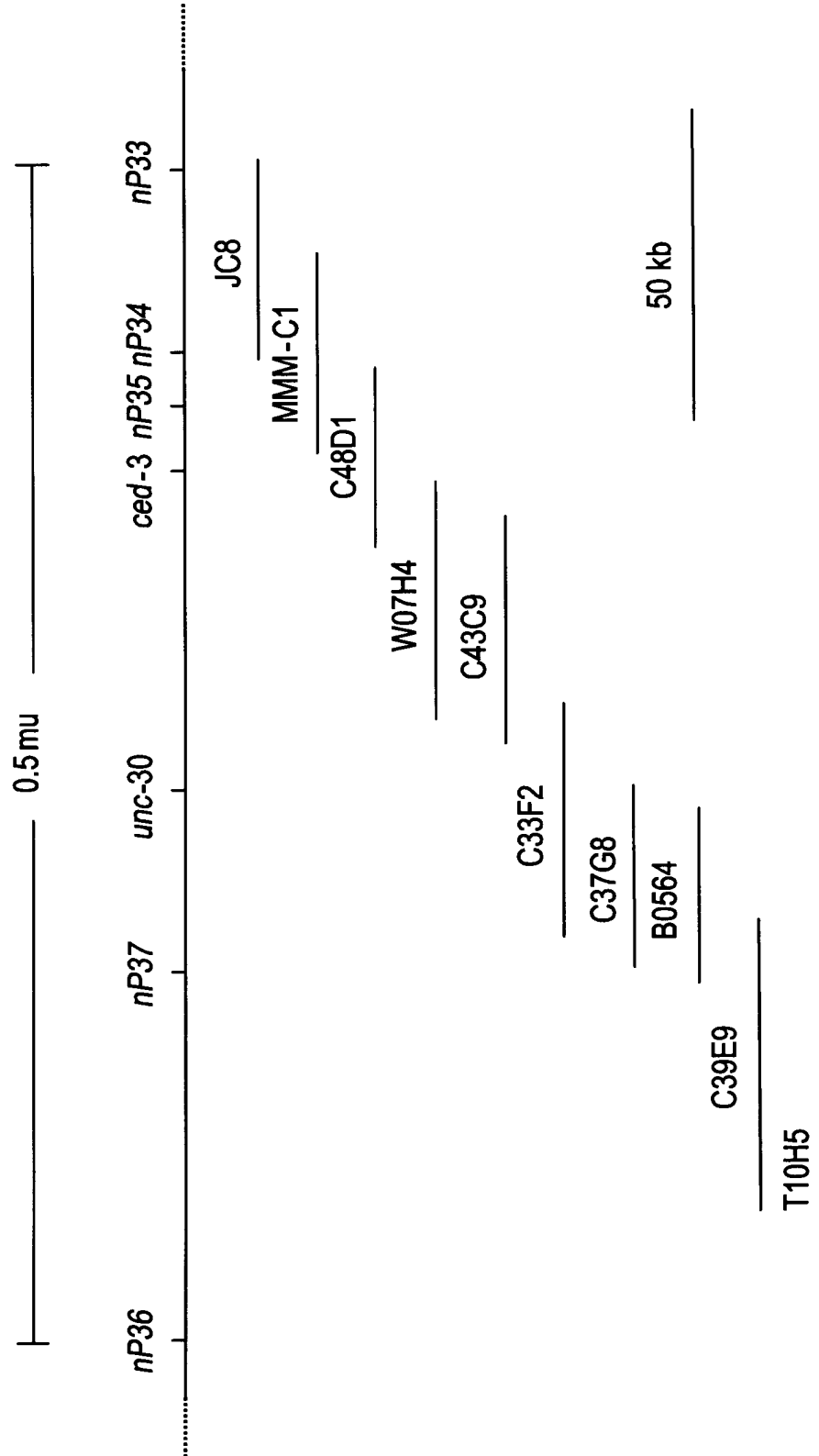
FIG. 8





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FIG. 9



Summary of the experiments to localize *ced-3* gene within C40D1

DNA	5kb			ced-3 activity	No. lines
C48D1	BamHI	BamHI	BamHI	++	2
C48D1-20	BamHI	BamHI BgIII	Apa1 BgIII BgIII BgIII	++	2
C48D1-43	BamHI	BamHI BgIII	Apa1 BgIII	++	1
pJ40	BamHI	BamHI BgIII	BgIII BgIII Apa1	++	1
pJ107	BamHI	BamHI BgIII	BgIII	++	1
pJ107del80 & pJ107del34	BgIII	BgIII	BgIII	++	3
pJ107del12 & pJ107del27	BgIII	BgIII	BgIII	+	1
pJ55 & pJ56	BamHI	BamHI BgIII	Sall	-	12